

# Importance of Pediatric Studies in SARS-CoV-2 Vaccine Development

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Vaccination efforts against COVID-19 must include the pediatric population, not only to protect children and their families from the virus, but also to support a safe return to in-person schooling. Given the novel methodologies and targets used in the COVID-19 vaccines and the potential for multisystem inflammatory syndrome-children, it is insufficient to extrapolate safety and efficacy data between different vaccine candidates or from adult studies. Adequate enrollment in pediatric studies for COVID-19 vaccines is crucial. The Pediatric Pharmacy Association supports continued research, surveillance, and transparency for COVID-19 vaccines in the pediatric population, including those younger than 12 years of age.

**ABBREVIATIONS** AAP, American Academy of Pediatrics; FDA, US Food and Drug Administration; MIS-C, multisystem inflammatory syndrome-children; PREA, Pediatric Research and Equity Act; SARS-CoV2, severe acute respiratory syndrome-corona virus-2

**KEYWORDS** COVID-19; pediatric; SARS-CoV2; vaccine

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## Background

Vaccines are essential to prevent the spread of disease. They have led to control and, in some cases, elimination of significant diseases such as polio, diphtheria, mumps, and rubella, among others. COVID-19 has had a devastating impact around the world, and vaccine development has taken place at record speeds. Although the true incidence of COVID-19 infection in children is unknown, over 3.2 million children have tested positive since the pandemic began.<sup>1,2</sup> Although current data have shown a lower incidence of severe illness as compared with adults, children are still at risk of developing severe disease and complications from COVID-19.<sup>1</sup> Information regarding how this disease affects children continues to evolve. Children with underlying medical conditions and/or compromised immune systems are at higher risk for severe illness from COVID-19.<sup>3</sup> Furthermore, little is known about the long-term sequelae following COVID-19 infection or complications such as multisystem inflammatory syndrome-children (MIS-C). The development of an effective COVID-19 vaccine is essential to mitigate the individual risks associated with children contracting COVID-19, as well as to decrease transmission throughout communities. As vaccines are approved, their efficient distribution and administration will be critical to ensure a safe return to school, work, and daily life. To accomplish this, it is vital to have well designed and sufficiently powered studies in both adult and pediatric populations.

## Issue

Although the specific rate of infection and likelihood of transmission continue to be undetermined, it is clear that children play a role in the transmission of severe acute respiratory syndrome-corona virus-2 (SARS-CoV2) and can themselves be infected with COVID-19.<sup>4</sup> In addition, almost one-quarter of the United States population are of pediatric age (0–18 years old), demonstrating the necessity for children to be included in any effective vaccination effort.<sup>5</sup> In order for children to safely be vaccinated, it is essential that they are included in SARS-CoV2 vaccine clinical trials. Not only are many of the SARS-CoV2 vaccines under development using a new target, but new methodologies have also been used to create the vaccines. Current vaccines, some of which are authorized for emergency use, employ novel mechanisms such as mRNA, replication-defective adenovirus vectors (i.e., human and chimpanzee), and nanoparticles.<sup>6</sup> These mechanisms have not been used in prior wide-scale vaccines, and data from one vaccine type cannot be easily extrapolated to others. Data from pediatric participants are needed to determine levels of antibody generation and safety, as these data cannot be reliably extrapolated from adult studies.

The American Academy of Pediatrics (AAP) and the US Food and Drug Administration (FDA) both cite the Pediatric Research and Equity Act (PREA) and encourage timely initiation of pediatric trials in the development of COVID-19 vaccines.<sup>6–8</sup> According to PREA, all medications, including vaccines, that have

potential benefit in children should be studied in this population.<sup>6</sup> PREA was enacted to ensure research in children is prioritized, as they may have differences in disease presentation and response to medications or biologics compared with adults. Children are much less likely to have acute COVID-19 disease; however, they are more likely to develop a multisystem inflammatory condition (i.e., MIS-C vs MIS-A).<sup>9</sup> This rare but significant postinfection presentation of COVID-19 in pediatric patients strengthens the need for safety studies of these vaccines in children.

Vaccine hesitancy must also be addressed to ensure children are enrolled in COVID-19 vaccine trials and receive vaccines once approved. Concerns about vaccine safety are often noted when parents refuse vaccines, and this presents an opportunity for the pharmacist to provide education.<sup>11</sup> The CEOs of several major pharmaceutical companies, including Moderna, Pfizer-BioNTech, and Janssen, released a statement in September 2020 ensuring that high scientific and ethical standards regarding the COVID-19 vaccine development process would not be compromised despite the accelerated timeline.<sup>12</sup> This commitment from the leadership of pharmaceutical companies promises transparency throughout vaccine development and clinical trials. Discussing this information with parents may help address any safety concerns and allow them to feel comfortable enrolling their children in the clinical trials.

## Position

**Recommendation 1.** When population immunity is necessary, as it is with COVID-19, it is important to study the vaccines in children to ensure their efficacy and safety.

Pfizer-BioNTech and Moderna have completed their vaccine trials in adolescents down to 12 years of age and Moderna has begun enrolling in their trial that will include patients 6 months to 12 years.<sup>13</sup> Janssen has announced their adolescent studies will begin in March 2021.<sup>10</sup> We applaud the FDA for encouraging sponsors to discuss pediatric drug development early in the approval process and we commend these pharmaceutical companies for their prompt initiation of adolescent studies. Further success of pediatric trials hinges not only on drug companies' continued commitment, but also on sufficient enrollment in these studies. Adequate patient enrollment will require pharmaceutical companies to set up sufficient trial sites across all regions of the country. In addition, educational programs provided by public health officials, professional organizations, and trusted health care providers can help improve parent and caregiver confidence in vaccine safety and allow them to feel comfortable enrolling their children in the trials. Emphasis should be placed on ensuring that education reaches minority communities, as the adult studies have had difficulty enrolling

this patient population. Without adequate educational outreach, the same could occur in pediatric trials. It is vital to study the vaccine in a diverse population so that efficacy and side effects can be generalized to the entire population.

**Recommendation 2.** The medical community can support enrollment in pediatric vaccine trials by providing resources to parents regarding the importance and safety of these studies.

Immunizations have a huge impact on patients' health. Over the last decade there has been a significant increase in vaccine hesitancy leading to alternative vaccine schedules and even refusal. It is imperative that pediatric health care providers engage in discussions with parents and caregivers to address their concerns. Discussions should include vaccine development and testing, assurance of vaccine safety, as well as the specific benefits provided by the vaccine and the risks associated with not receiving it.<sup>11</sup> This is especially important with the COVID-19 vaccines because many myths have been circulated in the lay press and on social media. Several resources are available to help with educating families.

## Resources

Useful informational resources for health care professionals and for families regarding COVID-19, vaccines, and various pediatric COVID-19 vaccine trials can be found in the Table.

## Conclusion

COVID-19 is a novel infection that has had a severe impact around the world. Although children may experience milder infections, they are not exempt from the devastating effects of COVID-19. Development of COVID-19 vaccines is imperative to control this worldwide outbreak and return to a sense of normalcy. The inclusion of pediatric patients is vital to achieving these goals. The Pediatric Pharmacy Association supports continued research, surveillance, and transparency for COVID-19 vaccines in the pediatric population, including those < 12 years of age. Hesitancy and misinformation surrounding the administration of COVID-19 vaccines are significant barriers to vaccination. Assuring the public that a vaccine is safe and effective is vital to immunizing a sufficient percentage of the population to counteract the rise of this pandemic.<sup>14</sup> The antivaccine movement has had a negative impact on current immunization rates, as evidenced by outbreaks of other vaccine-preventable diseases in recent years. Including children in ongoing research and surveillance will expand the body of evidence related to COVID-19 vaccine use, safety, and effectiveness, as well as inform current and future mass immunization efforts for people of all ages.<sup>14</sup> We encourage all health care professionals to address vaccine hesitancy and the common myths

**Table. Recommended Resources****General Immunization Information**

Healthcare professionals	<a href="https://www.cdc.gov/coronavirus/2019-ncov/vaccines/facts.html?CDC_AA_refVal=https%3A%2F%2Fwww.cdc.gov%2Fcoronavirus%2F2019-ncov%2Fvaccines%2Fvaccine-benefits%2Ffacts.html">https://www.cdc.gov/coronavirus/2019-ncov/vaccines/facts.html?CDC_AA_refVal=https%3A%2F%2Fwww.cdc.gov%2Fcoronavirus%2F2019-ncov%2Fvaccines%2Fvaccine-benefits%2Ffacts.html</a>
Parents and caregivers	<a href="https://www.fda.gov/vaccines-blood-biologics/consumers-biologics/vaccines-children-guide-parents-and-caregivers">https://www.fda.gov/vaccines-blood-biologics/consumers-biologics/vaccines-children-guide-parents-and-caregivers</a>

**Vaccine Hesitancy**

American Academy of Pediatrics	<a href="https://www.aap.org/en-us/advocacy-and-policy/aap-health-initiatives/immunizations/Pages/vaccine-hesitant-parents.aspx">https://www.aap.org/en-us/advocacy-and-policy/aap-health-initiatives/immunizations/Pages/vaccine-hesitant-parents.aspx</a> <a href="https://pediatrics.aappublications.org/content/pediatrics/138/3/e20162146.full.pdf">https://pediatrics.aappublications.org/content/pediatrics/138/3/e20162146.full.pdf</a>
Centers for Disease Control and Prevention	<a href="https://www.cdc.gov/vaccines/hcp/conversations/index.html">https://www.cdc.gov/vaccines/hcp/conversations/index.html</a>
Pediatric Pharmacy Association	McKee C, Bohannon K. Exploring the reasons behind parental refusal of vaccines. <i>J Pediatr Pharmacol Ther.</i> 2016;21(2):104–109. doi:10.5863/1551-6776-21.2.104
COVID-19 Vaccine: Myths and Facts	<a href="https://www.cdc.gov/coronavirus/2019-ncov/vaccines/facts.html?CDC_AA_refVal=https%3A%2F%2Fwww.cdc.gov%2Fcoronavirus%2F2019-ncov%2Fvaccines%2Fvaccine-benefits%2Ffacts.html">https://www.cdc.gov/coronavirus/2019-ncov/vaccines/facts.html?CDC_AA_refVal=https%3A%2F%2Fwww.cdc.gov%2Fcoronavirus%2F2019-ncov%2Fvaccines%2Fvaccine-benefits%2Ffacts.html</a>

**Pediatric Enrollment in COVID-19 Vaccine Clinical Trials**

Pfizer-BioNTech	<a href="https://www.Pfizer.com/science/clinical-trials/children">https://www.Pfizer.com/science/clinical-trials/children</a>
Moderna	<a href="https://connect.trialscope.com/studies/0e8fc8e6-5782-46fd-8b03-0994a5ad8b41">https://connect.trialscope.com/studies/0e8fc8e6-5782-46fd-8b03-0994a5ad8b41</a> <a href="https://clinicaltrials.gov/ct2/show/NCT04796896">https://clinicaltrials.gov/ct2/show/NCT04796896</a>

surrounding COVID-19 vaccines and to provide the necessary resources to parents and caregivers, so that they feel confident enrolling their children in vaccine clinical trials.

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**References**

- Centers for Disease Control and Prevention. Coronavirus Disease 2019 (COVID-19): Information for pediatric healthcare providers. Accessed March 5, 2021. <https://www.cdc.gov/coronavirus/2019-ncov/hcp/pediatric-hcp.html>
- American Academy of Pediatrics. Critical updates on COVID-19 - children and COVID-19: state-level data reports. Accessed March 12, 2021. <https://services.aap.org/en/pages/2019-novel-coronavirus-covid-19-infections/children-and-covid-19-state-level-data-report/>
- Centers for Disease Control and Prevention. Coronavirus Disease 2019 (COVID-19): people with certain medical conditions. Accessed March 5, 2021. <https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-with-medical-conditions.html>

4. Goldstein E, Lipsitch M, Cevik M. On the effect of age on the transmission of SARS-CoV-2 in households, schools and the community. *J Infect Dis*. 2021;13;223(3):362–369.
5. Census.gov. Age and sex composition: 2010: 2010 census briefs. Accessed October 30, 2020. <https://www.census.gov/prod/cen2010/briefs/c2010br-03.pdf>
6. World Health Organization. Draft landscape of COVID-19 candidate vaccines. Accessed October 30, 2020. <https://www.who.int/publications/m/item/draft-landscape-of-covid-19-candidate-vaccines>
7. Goza SH. AAP Letter to HHS and FDA Children COVID 19 Vaccine Trials. Received by Alex Azar and Stephen M. Hahn. September 29, 2020.
8. Food and Drug Administration. COVID-19: developing drugs and biological products for treatment or prevention guidance for industry. Accessed May 5, 2021. <https://www.fda.gov/regulatory-information/search-fda-guidance-documents/covid-19-developing-drugs-and-biological-products-treatment-or-prevention>
9. Feldstein LR, Rose EB, Horwitz SM, et al. Multisystem inflammatory syndrome in U.S. children and adolescents. *N Engl J Med*. 2020;383(4):334–346.
10. Neergaard L. Next up in hunt for COVID-19 vaccine: testing shots in kids. ABC News: Coronavirus. Accessed October 24, 2020. <https://abc7ny.com/coronavirus-covid-vaccine-testing/7301453/>
11. Edwards KM, Hackell JM; Committee on Infectious Diseases, the Committee on Practice and Ambulatory Medicine. Countering vaccine hesitancy. *Pediatrics*. 2016;138(3):e20162146. doi:0.1542/peds.2016-2146
12. The Wall Street Journal. Drug-company CEOs sign pledge on COVID-19 vaccine. Accessed November 2, 2020. <https://www.wsj.com/articles/nine-drug-company-ceos-sign-pledge-on-covid-19-vaccine-11599572714>.
13. Moderna. Moderna announces first participants dosed in phase 2/3 study of COVID-19 vaccine candidate in pediatric population. Accessed March 16, 2021. <https://investors.modernatx.com/news-releases/news-release-details/moderna-announces-first-participants-dosed-phase-23-study-0>
14. American Society of Health-System Pharmacists. ASHP principles for COVID-19 vaccine distribution, allocation, and mass immunization. Accessed November 2, 2020. <https://www.ashp.org/-/media/assets/pharmacy-practice/resource-centers/Coronavirus/docs/ASHP-Principles-for-COVID-19-Vaccine>